

22. A method of screening for a candidate substance which inhibits the phosphorylation of a tau protein by casein kinase 1 (CK1), the method comprising:

(a) contacting

i) said candidate substance;

ii) a tau protein comprising the amino acid sequence of SEQ ID NO:2, or a tau variant comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:2, said tau protein or tau variant including the phosphorylation sites S46, T50, S113, S131, T149, T169, S184, S208, S210, T212, S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, S412, S413, T414, S416, S433 and S435, said phosphorylation sites corresponding to the amino acid sequence of SEQ ID NO:2;

iii) a CK1 polypeptide comprising the amino acid sequence of SEQ ID NO: 1, or a CK1 variant comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1, wherein said CK1 polypeptide or CK1 variant phosphorylates the tau protein or the tau variant of ii) at (S46/T50), S113, S131, T149, T169, S184, S208, (S210/T212), S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, (S412/S413/T414), S416, S433 or S435 corresponding to the amino acid sequence of SEQ ID NO:2;

(b) determining whether, and optionally the extent to which the candidate substance of i) inhibits phosphorylation of the tau protein or tau variant of ii) by the CK1 polypeptide or CK1 variant of iii) at (S46/T50), S113, S131, T149, T169, S184, S208, (S210/T212), S214, S237, S238, S241, S258, S262, T263, S285, S289, S305, S341, S352, S356, T361, T373, T386, (S412/S413/T414), S416, S433 or S435 corresponding to the amino acid sequence of SEQ ID NO:2; and

(c) selecting the candidate substance that inhibits phosphorylation of said tau protein or tau variant at one or more phosphorylation sites.